

2013 Indiana Healthcare Provider and Hospital Administrator Multi-Drug Resistant Organism Survey

Antibiotic resistance is a global issue that has significant impact in the field of infectious diseases. It has been recognized for several decades that up to 50% of antibiotic use is either inappropriate or unnecessary. Antibiotics are the only drugs where use in one patient can impact the effectiveness in another. Recent cases and outbreaks of antibiotic resistant organisms, including methicillin resistant *Staphylococcus aureus* (MRSA), *Clostridium difficile* infection (CDI), extremely-drug resistant tuberculosis (XDR-TB), and carbapenemase-resistant *Enterobacteriaceae* (CRE), have shown that antibiotic resistance represents a serious threat to public health. These organisms are associated with high mortality rates and have the potential to spread widely. They also represent a significant burden to the health care system. Improving antibiotic use is a public health imperative.

Pharmaceutical companies are minimally involved in the development of antibiotics. From 1983-1987, sixteen new antibiotics were approved by the US Food and Drug Administration (FDA). However, from 2008-2011 only two new antibiotics were approved and neither addressed the issue of resistance. In 1990, nineteen companies developed antibiotics, but presently only four produce them. It will be five to ten years before new antibiotics are available to treat resistant organisms.

Given this lack of new antibiotics to treat multi-drug resistant organism (MDRO) infections, an aggressive infection control strategy is critical to prevent the transmission of these resistant organisms. Early detection and implementation of strict infection control measures can prevent MDROs in healthcare facilities (HCFs) from becoming a more significant threat to patients. Following contact precautions, using antibiotics wisely and minimizing device usage are all important aspects of preventing transmission. These core measures are located in the Centers for Disease Control and Prevention (CDC) Healthcare Infection Control Practices Advisory Committee (HICPAC) Guidelines, "Management of Multidrug-Resistant Organisms in Healthcare Settings, 2006" (http://www.cdc.gov/hicpac/mdro/mdro_toc.html).

Klebsiella pneumoniae and *Escherichia coli*, which are included in the family of gram-negative bacteria known as *Enterobacteriaceae*, are epidemiologically and clinically important organisms due to their level of antibiotic resistance. The carbapenem-resistant strains of these organisms are referred to as carbapenem-resistant *Enterobacteriaceae* (CRE). Types of CRE are known as *Klebsiella pneumoniae* carbapenemase (KPC) and New Delhi Metallo-beta-lactamase (NDM). CRE are an emerging, important healthcare challenge, resistant to almost all current available antibiotics and have been associated with high mortality rates (up to 40 to 50% in some studies). The gene that confers this resistance pattern is contained on plasmids, which are highly mobile and very easily spread from one bacterial cell to the next. Since these cells are harbored in the gut, the plasmids are potentially transferrable to multiple coliforms. The CDC reports CRE infections have increased from 1% to 4% in the past decade.

Healthcare providers should be concerned about CRE infections as they are associated with high rates of morbidity and mortality, serious treatment challenges, increased length of stay, and increased cost. The frequent movement of patients between acute and long term care facilities provides the opportunity for transmission of these resistant organisms. Aggressive communication between both acute and long term care facilities is important so that appropriate intervention can take place. Further detailed guidance developed by the CDC designed to decrease transmission of CRE is located in the "2012 CRE Prevention Toolkit" at <http://www.cdc.gov/hai/pdfs/cre/CRE-guidance-508.pdf>.

To slow the evolution of resistance, healthcare providers must focus on antibiotic stewardship. Stewardship programs will enforce pathogen-directed therapy and short-course treatment. In a recent study the CDC reported that exposure to a carbapenem antibiotic increased a patient's risk of getting an infection with a carbapenem-resistant strain by 15 times. When ordering antibiotics healthcare providers are encouraged to select appropriately for specific dose, duration, route and indication. Antibiotic use should be reassessed after 24 to 48 hours to review susceptibility results and determine if treatment can be altered. Further detailed guidance describing the development of an antibiotic stewardship program from the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA) is located at "Guidelines for Developing an Institutional Program to Enhance Antimicrobial Stewardship" <http://cid.oxfordjournals.org/content/44/2/159.full>.

Microbiology laboratories in all acute care facilities must implement enhanced protocols to detect carbapenemase production in *Enterobacteriaceae*. When these organisms are identified the laboratory must immediately alert acute and long term care Infection Preventionists (IPs). This will allow important control measures to be implemented, including vigorous hand hygiene practices, contact precautions, and minimizing the use of devices.

The Indiana State Department of Health (ISDH) strives to heighten awareness of the challenges posed by antibiotic resistance. The combination of a comprehensive infection prevention program and effective antibiotic stewardship will minimize the emergence and transmission of MDROs in Indiana. In order to better understand the current HCF infection control practices and CRE detection practices in Indiana, the ISDH Surveillance and Investigation Division (SID) and the ISDH Laboratory partnered to repeat surveys that were originally sent to IPs and clinical laboratories in 2011. The results from both surveys are located at <http://www.in.gov/isdh/25507.htm>.

To further address this major public health threat, the ISDH, in collaboration with Marion County Public Health Department, Indiana Hospital Association, Association for Professionals in Infection Control and Epidemiology (Indiana Chapter), IU Health, and the new Wishard Eskenazi Health Hospital, has convened the Indiana Antibiotic Resistance Advisory Committee.

Healthcare providers (HCP) and hospital administrators recently were asked to complete a survey via Survey Monkey to assess knowledge, attitudes, and practices

regarding antibiotic prescribing, antibiotic stewardship, and facility level prevention strategies, such as hand hygiene, infection control interventions, laboratory testing, and surveillance cultures. Responses to this survey will provide data to describe antibiotic resistance in Indiana and allow the Committee to identify priorities for educational resources, tools, and best practices. The results from this survey are summarized below.

Indiana Healthcare Provider and Hospital Administrator
Multi-Drug Resistant Organism Survey

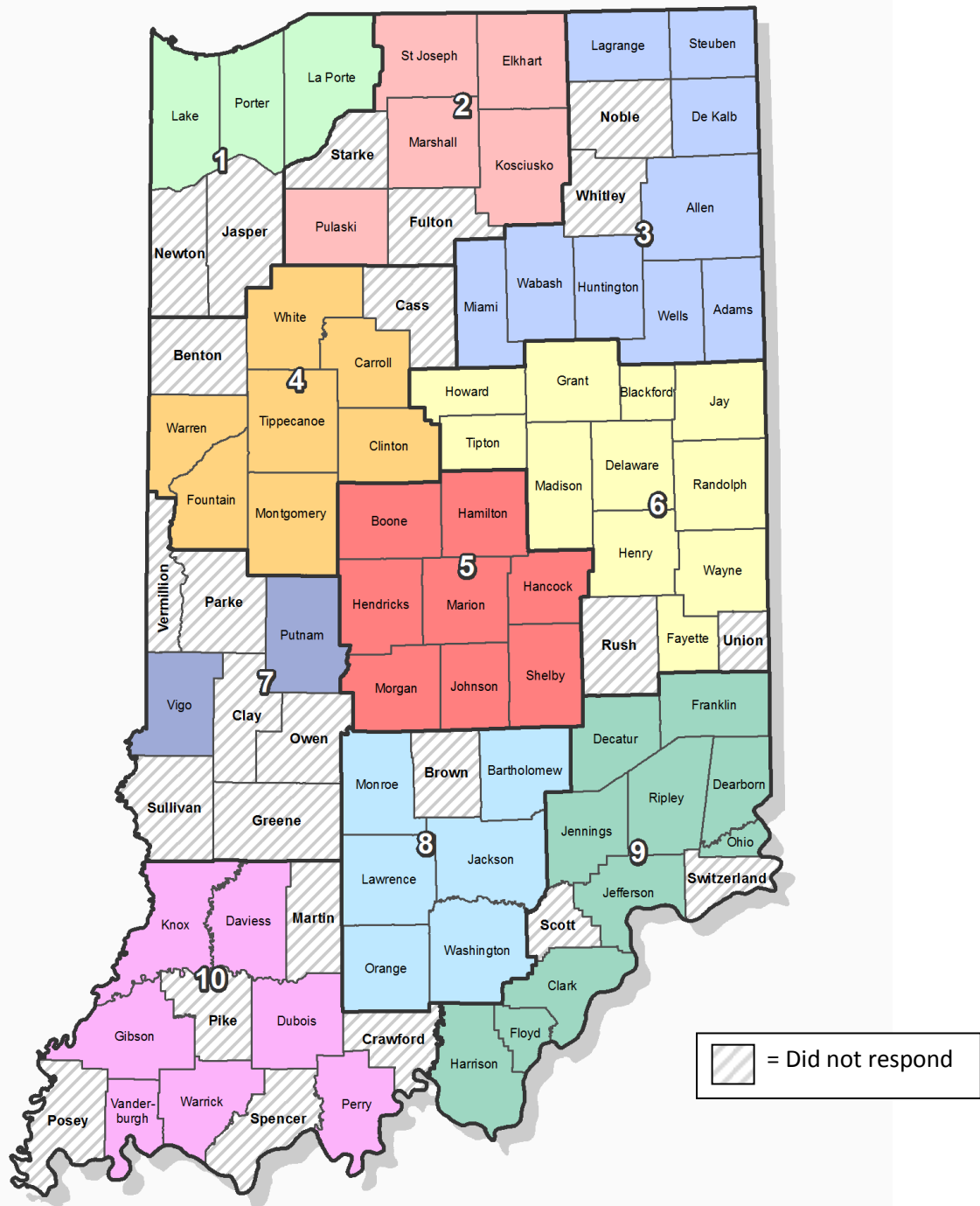
On June 17, 2013, the Indiana Antibiotic Resistance Advisory Committee conducted a survey of Healthcare Providers and Facility Administrators to assess awareness of treatment, prevention and antibiotic stewardship regarding MDROs in Indiana. The survey consisted of a series of questions in 3 Categories; Demographic (8 questions), Knowledge of CRE (9 questions), and Attitudes or Beliefs about Potential Strategies to Control MDRO (10 questions). The survey was provided in electronic format through Survey Monkey website, with a total of 614 individuals responding. Data was excluded from 142 individuals as 106 provided only demographic data and 36 responses were from out of state. Therefore, the data used for analysis involved responses from 472 individuals. No survey questions were mandatory allowing for differences in the response rate.

Demographic Information

The largest professional group to respond were MD's in the 51-60 year age range who indicated they have practiced for >30 years. Family Practice was reported most often as the specific specialty area of medicine practiced. Survey responses were received from 68 Indiana counties and no response from 24 counties as indicated on map below. The top six counties which responded were; Marion, Hamilton, Vanderburgh, Allen, St. Joseph, and Lake. When asked in the past 12 months how many patients were known to be colonized or infected with CRE, 80% indicated they were aware of no CRE patients.

| County | Number of Responses |
|-------------|---------------------|
| Marion | 152 |
| Hamilton | 26 |
| Vanderburgh | 18 |
| Allen | 17 |
| St. Joseph | 17 |
| Lake | 16 |

Map of Responding Indiana Counties



Knowledge of CRE

The Antibiotic Resistance Advisory Committee developed the next set of 9 questions referencing the "2012 CDC Guidance for Control of CRE" to determine the HCP and HCF Administrator's knowledge of CRE. Response values were reported as True, False or Not Sure.

The main risk factors for CRE acquisition include exposure to healthcare and exposure to antibiotics. CRE infections have been associated with high rates of morbidity and mortality. When asked if "The majority of CRE infections have occurred in patients with substantial healthcare exposure", 56% responded were not sure and 7% believed statement to be false.

CRE organisms have developed resistance to multiple classes of antibiotics, including last-resort drugs called carbapenems, therefore substantially limiting treatment options. When asked if "Microbiology reports for CRE cases typically reveal resistance to all commonly used antibacterial agents", 30% responded were not sure and 8% believed statement to be false.

The current CRE surveillance definition is based upon the January 2012 CLSI M100-S22 interpretative criteria. The survey response indicated 74% were not sure of CRE testing method performed at their HCF and 8% stated this was not the test used.

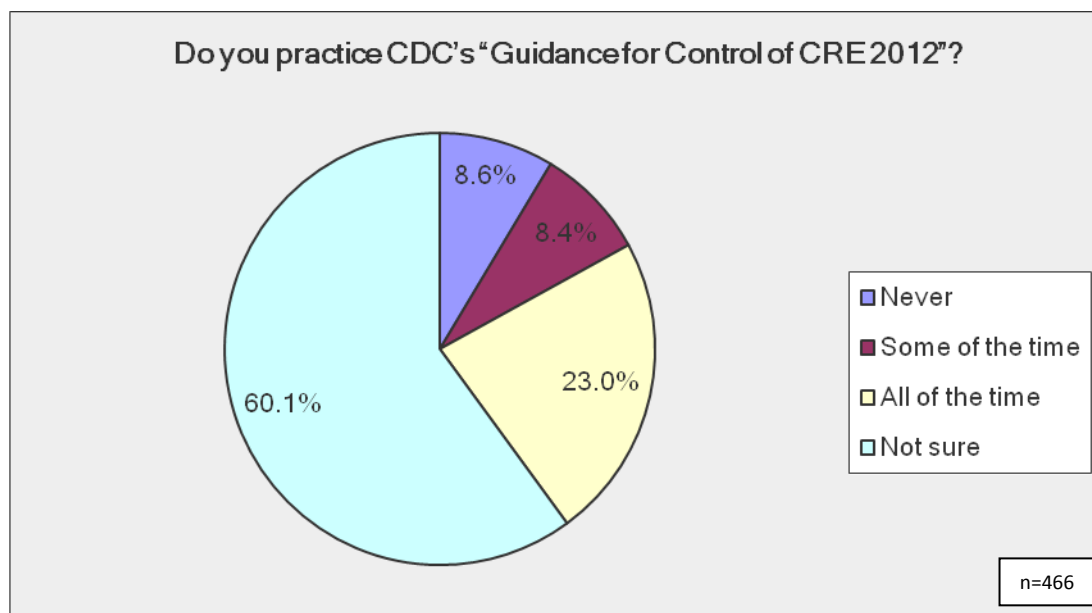
Pharmaceutical companies are no longer interested in the development of antibiotics. From 1983-1987, sixteen new antibiotics were approved by the FDA, but from 2008-2011 only two new antibiotics were approved and neither addressed the issue of resistance. When asked if "Antibacterial agents with activity against CRE are currently in advanced stages of clinical development and will be available for clinical use soon", 60% responded were not sure.

When found in clinical culture, CRE can represent an infection or colonization. Colonization means that the organism can be found on the body but it is not causing any symptoms or disease. Colonizing CRE strains can go on to cause infections if they gain access to body sites that are usually sterile like the bladder, the lungs, or the bloodstream. When asked if "Persons may be carriers of CRE for extended periods of time and have no symptoms of active infection", 31% responded were not sure and 67% agree that statement was true.

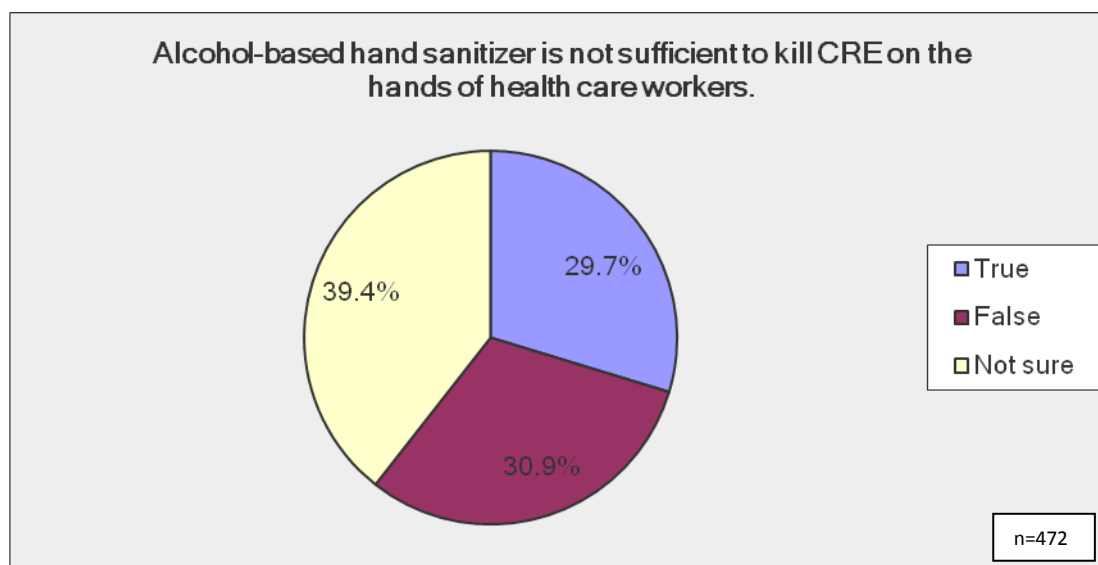
CRE can become nonsusceptible to carbapenems due to a number of mechanisms. Most carbapenem resistance mediated by carbapenemases in the U.S. is found among *Klebsiella* spp. and *E. coli*. The genes that code for KPC are on a highly mobile genetic element that can be transmitted from one bacterium to another thereby spreading resistance. The survey response indicated 52% were not sure regarding CRE resistance mechanisms.

The CDC has provided multiple promotional forms involving CRE education such as, the "2012 Guidance for Control of CRE" which expanded upon the March 2009 guidance, the

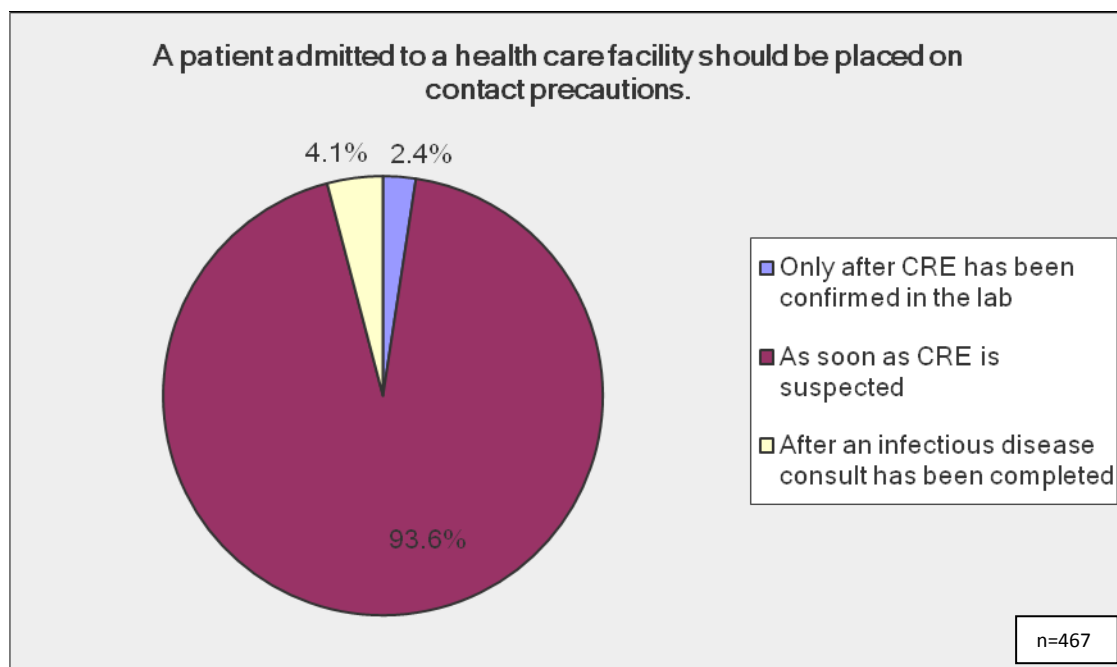
enhancement of CRE web page, and featuring CRE in the "Vital Signs" March 2013. In addition, the ISDH created a CRE web page, Quick Facts and articles in the ERC Weekly Digest and Epi Newsletter highlighting the CDC CRE guidelines. When asked "Do you practice CDC's "2012 Guidance for Control of CRE" responses are demonstrated below.



Hand hygiene is the single most effective means of preventing MDRO transmission. Facilities should have policies that require hand hygiene; monitor adherence rates; and ensure access to adequate hand hygiene stations (i.e., clean sinks and/or alcohol-based hand rubs). Survey response to hand hygiene practice is demonstrated below.



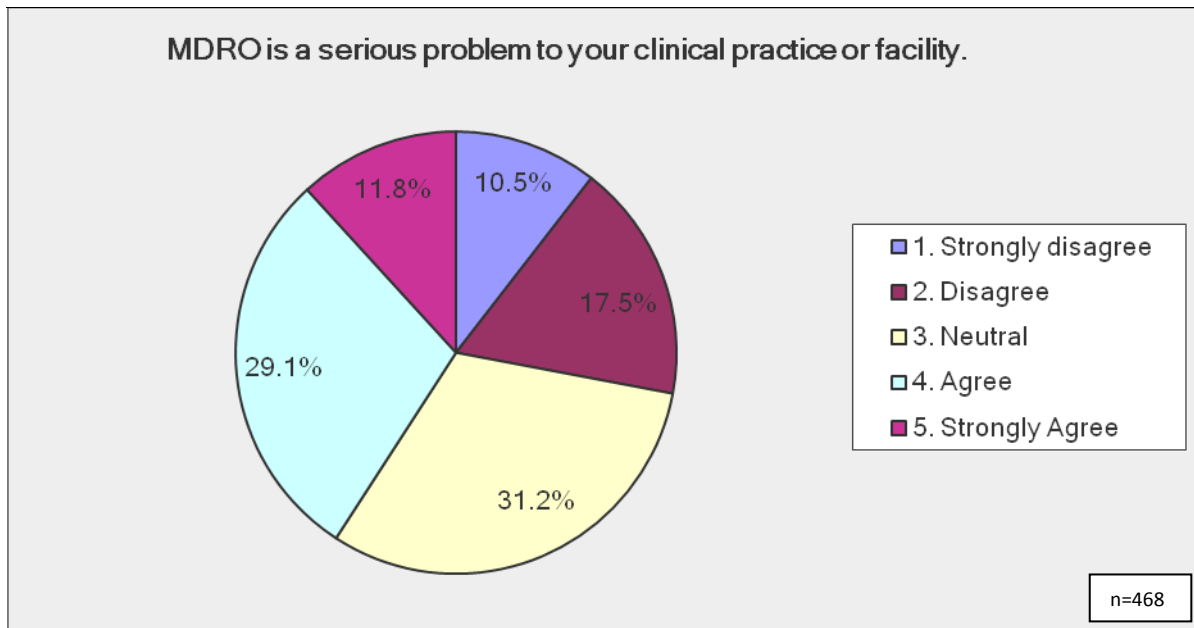
Patients colonized or infected with CRE in acute care settings should be placed on Contact Precautions. In long-term care settings, Contact Precautions are still indicated for residents infected or colonized with CRE but might be modified. Facilities should ensure proper use and rationale for Contact Precautions including the monitoring and surveillance. Survey response to use of Contact Precautions is demonstrated below.



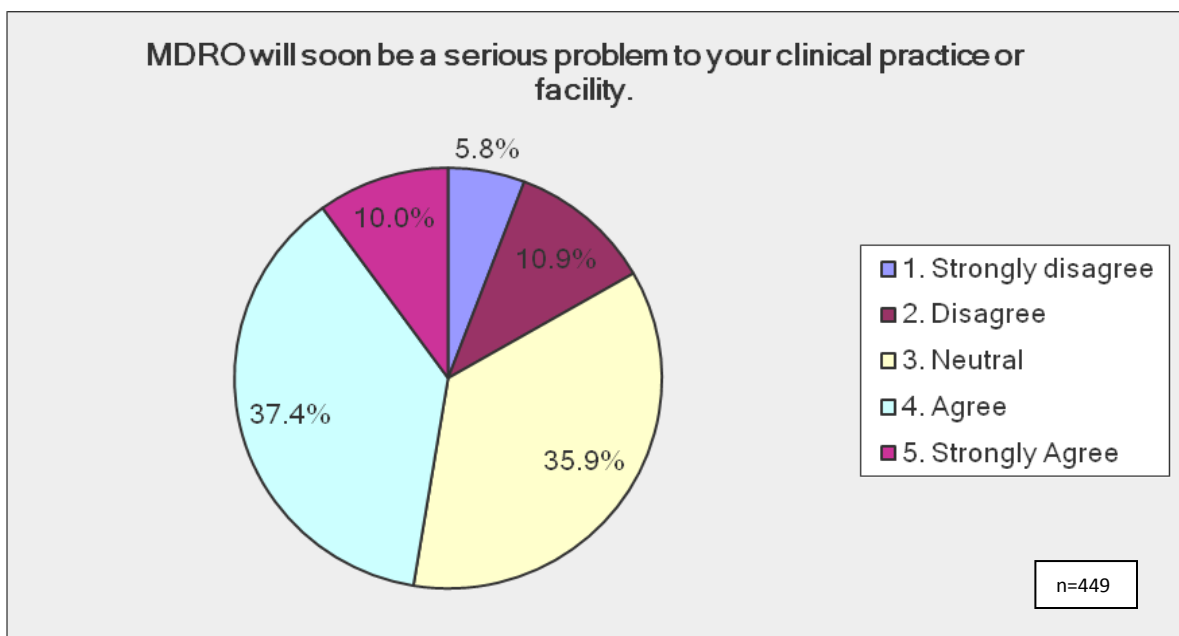
Strategies to Control MDRO

The Antibiotic Resistance Advisory Committee developed the next set of 10 questions to determine the HCP and HCF Administrator's attitudes and beliefs about potential strategies to control MDRO. Response values were reported as strongly disagree, disagree, neutral, agree, or strongly agree. If response was agree or strongly agree the individual was asked to provide a response detailing the specific organisms or infections that present the greatest challenge.

Survey response to the frequency of a patient presenting with a MDRO is demonstrated below. The organism or infection presenting the greatest challenge was reported as MRSA (74%) followed by CDI (49%).



HCP and HCF Administrator's response is demonstrated below when asked if MDRO were considered as a potential future problem. Those concerned of MDRO occurrence were prompted to explain what specific reason was a contributing factor. Free text responses included: the overuse of antibiotics, misuse of broad spectrum antibiotics, lack of new antibiotics, and poor hand hygiene compliance.

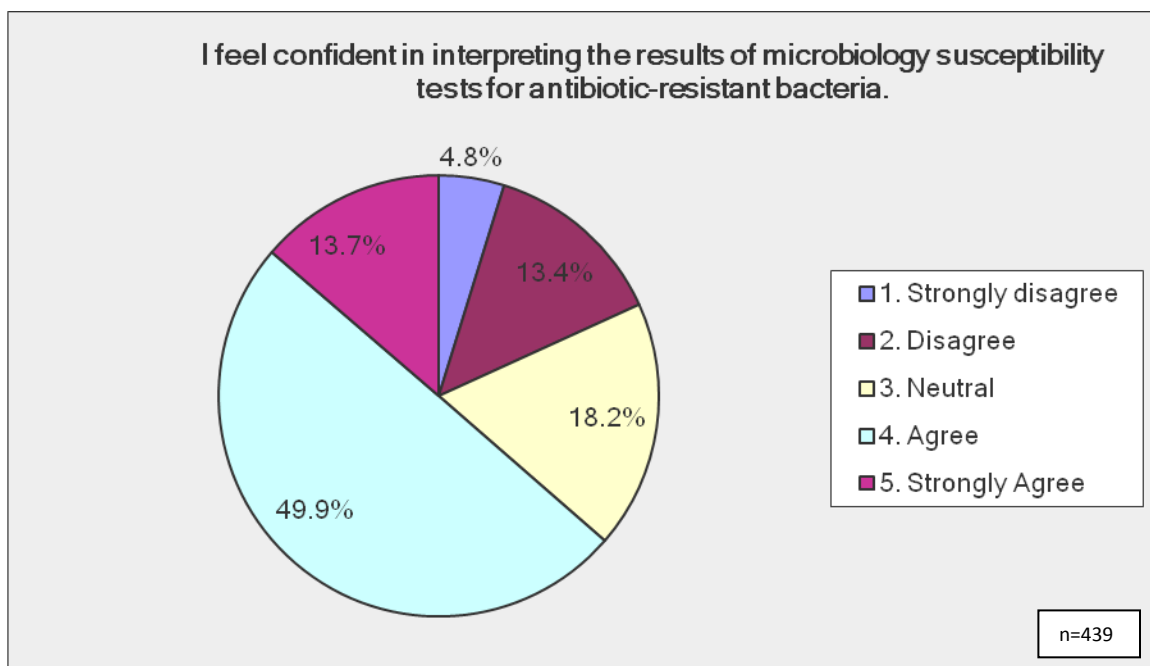


The majority of survey response supported strict adherence to hand hygiene and Contact Precautions as key to prevention of MDRO transmission. Although 3% strongly disagreed, 4% disagreed and 15% were neutral.

The majority of survey response agreed the judicious use of antibiotics and an effective antibiotic stewardship program would minimize the dissemination of antibiotic resistant bacteria.

The majority of survey response requested more MDRO infection prevention and antibiotic stewardship program education.

Confidence in the interpretation of MDRO laboratory results was reported as demonstrated below.

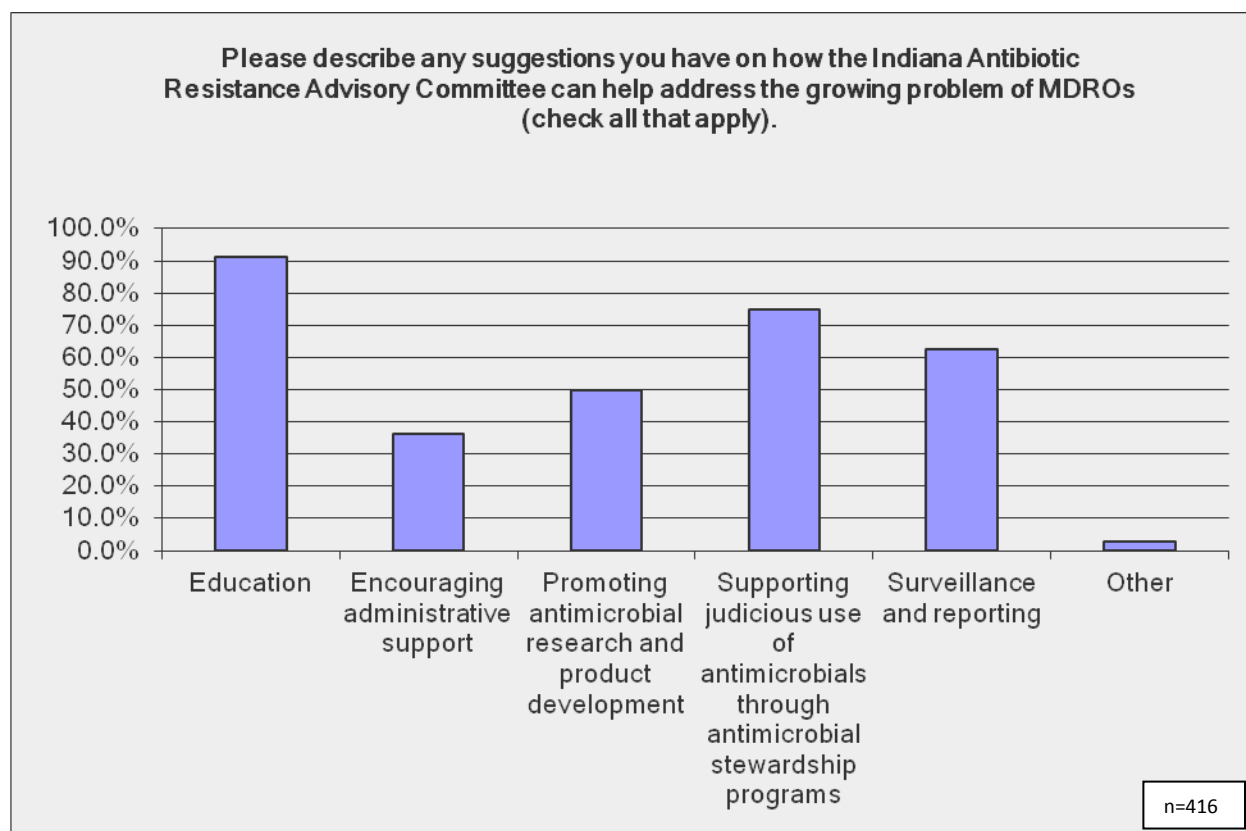


The majority of survey response agreed with easy access to an infectious disease specialist for assistance in treatment of a MDRO infected patient. Although 11% strongly disagreed, 15% disagreed and 13% were neutral.

Free text survey response to any MDRO challenges included: education of patients regarding antibiotic use, adherence to hand hygiene and Contact Precautions, pressure from colleagues to treat with antibiotics, negative patient satisfaction survey influence due to decreased antibiotic use, lack of antibiotic stewardship program, and the early recognition of MDRO.

Survey response to improving MDRO occurrence was reported as demonstrated below. Additional free text suggestions included: better education to general public

demanding antibiotics, less emphasis on patient satisfaction score and more on antibiotic stewardship, standard isolation practices, better communication between acute and long term care facilities, and support when antibiotics are not prescribed.



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